

Combined Efficacy of Acamprosate and Disulfiram in the Treatment of Alcoholism: A Controlled Study

Jacques Besson, François Aubry, Antoine Kasse, Philippe Leheret, and Adriaen Potgieter

This study presents the results of a multicenter investigation of the efficacy of acamprosate in the treatment of patients with chronic or episodic alcohol dependence. One hundred eighteen patients were randomly assigned to either placebo or acamprosate, and both groups were stratified for concomitant voluntary use of disulfiram. Treatment lasted for 360 days, with an additional 360-day follow-up period. The primary efficacy parameters evaluated were: relapse rate and cumulative abstinence duration (CAD). Results were analyzed according to Intention-To-Treat principles using χ^2 , *t*, and multiple regression analyses where appropriate. After 36 days on study medication, 40 of 55 (73%) acamprosate-treated patients were abstinent, compared with 26 of 55 (47%) placebo-treated patients ($p = 0.019$). The treatment advantage remained throughout the study medication period and was statistically significant until day 270 ($p = 0.028$). Twenty-seven percent of patients on acamprosate and 54% of patients on placebo had a first drink within the first 30 days of the study. The mean CAD was 137 days (60% abstinent days) for the patients treated with acamprosate and 75 days (21% abstinent days) for the placebo group ($p = 0.013$). No adverse interaction between acamprosate and disulfiram occurred, and the subgroup who received both medications had a better outcome on CAD than the those on only one or no medication. Acamprosate was well tolerated. Diarrhea was the only significant treatment-induced effect. It was concluded that acamprosate was a useful and safe pharmacotherapy in the long-term treatment of alcoholism. Concomitant administration of disulfiram improved the effectiveness of acamprosate.

Key Words: Relapse Prevention, Alcohol Dependence, Acamprosate, Disulfiram.

ALCOHOLISM IS one of the most commonly seen clinical psychiatric syndromes in Western countries,¹ and Switzerland is no exception.² Despite its high prevalence, there is no generally recognized specific pharmacotherapy for alcoholism.³ A large controlled multicenter study⁴ with disulfiram (antabuse), the most widely available pharmacotherapy used to promote abstinence from alcohol, failed to demonstrate its efficacy versus either a placebo or an medication, as regards in the rate or duration of abstinence, employment, or social stability. Among those patients who drank, however, the active medication was associated with a reduction in the number of days of drinking.

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Other pharmacotherapeutic agents have also been found to be of limited use in the treatment of alcoholism. Serotonergic antidepressants seem to be helpful in diminishing the desire to drink (at least for short periods) and the actual consumption of alcohol in both animals and humans.⁵ Naltrexone (recently marketed in the United States for this indication), is an opiate antagonist that showed moderate success in reducing relapses over 12 weeks.⁶ The effect was reinforced by the concomitant use of cognitive skills therapy,⁷ but data on continuous long-term abstinence has not yet been published.

Acamprosate, a homotaurine derivative, is a new synthetic compound whose chemical structure is related to that of taurine and γ -aminobutyric acid (GABA),⁸ both of which are neurotransmitters. Research has demonstrated that acamprosate displaces GABA bound to GABA_A and GABA_B receptors *in vitro*, and that it reduces cerebellar cGMP concentrations *in vivo*.⁹ Acamprosate also increases the number of GABA receptor sites and modifies the affinity of the carrier proteins, as well as the extent of binding of GABA in different cerebellar structures.¹⁰ Recent studies indicate that acamprosate also acts as inhibitory, by effect of excitatory amino acids in the rat neocortex.¹¹ The results of these studies suggest that acamprosate crosses the blood-brain barrier and acts on inhibitory, as well as excitatory, amino acids, producing a marked reduction in alcohol consumption in animals.¹²

In animal pharmacological studies, acamprosate did not demonstrate any hypnotic, anxiolytic, or muscle-relaxant properties,¹³ which distinguishes it from barbiturates and benzodiazepines. Acamprosate also proved to be inactive in studies for detecting an antidepressant activity. Acamprosate does not influence several measures of alcohol toxicity.¹⁴

In an initial double blind, placebo-controlled study of 85 alcoholic patients in withdrawal, 53% of the acamprosate patients relapsed within 3 months against 66% of the placebo patients.¹⁵ Several subsequent studies in France,¹⁶ Belgium,¹⁷ and Germany¹⁸ reported a positive therapeutic effect with acamprosate in maintaining abstinence in alcohol-dependent patients over periods up to 2 years.

The purpose of the present study was to evaluate the efficacy and safety of acamprosate in maintaining abstinence in treated alcoholics during a 360-day treatment period, with a 360-day follow-up period. Due to the frequent use of disulfiram in Switzerland, concomitant pre-

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LSD and Alcoholism Arnold M. Ludwig, Jerome Levine, Louis H. Stark, 1970 **LSD and Alcoholism** Arnold M. Ludwig, Jerome Levine, Louis H. Stark, 1970 *The Effectiveness and Costs of Alcoholism Treatment* Leonard Saxe, United States. Congress. Office of Technology Assessment, 1983 *Research on Alcoholism : Clinical Problems and Special Populations* Alcoholism Conference 1st, Washington, D. C., 1971, 1973 *Ecstasy: The Clinical, Pharmacological and Neurotoxicological Effects of the Drug MDMA* Stephen J. Peroutka, 2012-12-06

The variety of viewpoints expressed in this book illustrate the many controversies surrounding MDMA. 1 On the one hand the proponents of MDMA use believe this agent offers a unique psychoactive effect that may have important clinical applications especially in the field of psychotherapy. On the other hand the scientific data concerning the neurotoxic effects of the drug are unequivocal. The most striking feature of the human information of MDMA is the paucity of data that has been generated on the drug since it was patented in 1914. As pointed out by Beck Chapter 6 and others a clear need exists for better epidemiological and clinical data on MDMA. In the absence of such data arguments both for and against the continued use of MDMA with humans will be difficult to support. Unfortunately the currently available data must be used to develop rational policies for potential human users of MDMA. At the present time there are no data indicating that recreational doses of MDMA permanently damage the human brain. Nonetheless based on a review of the contents of this book as well as on informal discussions with approximately 200 recreational users of MDMA the following personal observations suggest that MDMA is radically different from other recreational drugs.

The Psychedelic Policy Quagmire J. Harold Ellens, Thomas B. Roberts Ph.D., 2015-08-18

Edited by two preeminent scholars this book provides coverage of the policy issues related to the increasingly diverse treatments practices and applications of psychedelics. Hallucinogenic substances like LSD, mescaline, peyote, MDMA and ayahuasca have a reputation as harmful substances that are enjoyed only by recreational users committing criminal acts. But leading international researchers and scholars who contributed to this book hold that the use of psychedelic substances for health, religious, intellectual and artistic purposes is a Constitutional right and a human right. Based on that conclusion these scholars focus on policy issues that regulate the use of psychedelic drugs in medicine, religion, personal life and higher education, arguing that existing regulations should match current and anticipated future uses. This volume has two parts. The first surveys research on the use of psychedelic drugs in medicine, religion and truth seeking, following these topics through history and contemporary practice. The second section treats government policies that regulate the psychological, physiological, biochemical and spiritual aspects of research and experience in these fields.

The Psychedelic Policy Quagmire Health Law Freedom and Society challenges medical and legal policy experts, ethicists, scientists and scholars with the question: How can we formulate policies that reduce the dangers of psychedelics misuse and at the same time maximize the emerging diverse benefits?

The Biology of Alcoholism Benjamin Kissin, Henri Begleiter, 2013-03-09

In this volume the

third of our series the emphasis has shifted from the theoretical and experimental to the more clinical and practical aspects of alcoholism Where in the earlier volumes more attention was directed to animal than human studies in this volume almost all material deals with the human condition The clinical manifestations of alcoholism may be divided into two major aspects that of the disease itself and that of its complications This separation is to some extent artificial since in a sense the natural history of the disease is a function of the development of certain complicating mechanisms These mechanisms in turn either become part and parcel of the underlying condition alcoholism or give rise to a new set of clinical variables characterized as medical complications At this point the dichotomy becomes real The disease alcoholism tends to be seen as a distinct psychosocial entity and to be treated with psychosocial techniques The medical complications are more clearly envisioned as being within the legitimate domain of medical practice and are treated by physicians who often tend to ignore the underlying alcoholism The patient is sometimes lost in between The major thrust of this volume is an attempt to describe the mechanisms of alcoholism as they are now known in such a way as to establish a continuum between the disease alcoholism and its medical complications

Sybil Exposed Debbie Nathan, 2012-06-12 Journalist Debbie Nathan reveals the true story behind the famous case of Sybil the woman with sixteen different personalities

Special Report to the U.S. Congress on Alcohol and Health from the Secretary of Health and Human Services, 1971

Acid Revival Danielle Giffort, 2020-07-21 A vivid analysis of the history and revival of clinical psychedelic science Psychedelic drugs are making a comeback In the mid twentieth century scientists actively studied the potential of drugs like LSD and psilocybin for treating mental health problems After a decades long hiatus researchers are once again testing how effective these drugs are in relieving symptoms for a wide variety of psychiatric conditions from depression and obsessive compulsive disorder to posttraumatic stress disorder and substance addiction In Acid Revival Danielle Giffort examines how this new generation of researchers and their allies are working to rehabilitate psychedelic drugs and to usher in a new era of psychedelic medicine As this team of researchers and mental health professionals revive the field of psychedelic science they are haunted by the past and by one person in particular psychedelic evangelist Timothy Leary Drawing on extensive archival research and interviews with people working on scientific psychedelia Giffort shows how today's researchers tell stories about Leary as an impure scientist and perform his antithesis to address a series of lingering dilemmas that threaten to rupture their budding legitimacy Acid Revival presents new information about the so called psychedelic renaissance and highlights the cultural work involved with the reassembly of dormant areas of medical science This colorful and accessible history of the rise fall and reemergence of psychedelic medicine is infused with intriguing narratives and personalities a story for popular science aficionados as well as for scholars of the history of science and medicine

Special Report to the U.S. Congress on Alcohol & Health from the Secretary of Health, Education, and Welfare United States. Department of Health,

Education, and Welfare, 1974

Alcoholism treatment & rehabilitation ; selected abstracts Information Planning

Associates,1972 **Alcoholism Treatment and Rehabilitation** National Institute of Mental Health (U.S.),1972 438
 references to worldwide literature published from 1960 to Sept 1971 but mostly from 1964 Materials selected to show broad
 range of treatment modalities treatment and rehabilitation programs and innovative techniques and methods Classified
 arrangement Foreign language titles also given in original Author index Subject index *Second Special Report to the U.S.*
Congress on Alcohol and Health National Institute on Alcohol Abuse and Alcoholism (U.S.),1975 **Integrative Addiction**
and Recovery Shahla Modir,George Munoz,2018-11-13 Integrative Addiction and Recovery is the most comprehensive
 textbook available on the research and clinical application of holistic approaches for treating substance use disorders
 Authored by world class experts in the field it presents both scientific and holistic data regarding a wide variety of holistic
 and conventional approaches to the treatment of substance abuse and behavioral addictions **National Library of**
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 (U.S.),1979 First multi year cumulation covers six years 1965 70 **Handbook of Medical Hallucinogens** Charles S.
 Grob,Jim Grigsby,2022-11-07 This handbook reviews promising applications of psychedelics in treatment of such challenging
 psychiatric problems as posttraumatic stress disorder major depression substance use disorders and end of life anxiety
 Experts from multiple disciplines synthesize current knowledge on psilocybin MDMA ketamine and other medical
 hallucinogens The volume comprehensively examines these substances neurobiological mechanisms clinical effects
 therapeutic potential risks and anthropological and historical contexts Coverage ranges from basic science to practical
 clinical considerations including patient screening and selection dosages and routes of administration how psychedelic
 assisted sessions are structured and conducted and management of adverse reactions **Second Special Report to the**
U.S. Congress on Alcohol & Health United States. Public Health Service,National Institute on Alcohol Abuse and
 Alcoholism (U.S.),1974 *Treatment and Rehabilitation of the Chronic Alcoholic* Benjamin Kissin,2012-12-06 The present
 volume contains a large variety of treatment approaches to the long term rehabilitation of the alcoholic ranging from the
 biological to the physiological to the psychological to the social The multiplicity of proposed therapies each of which has its
 strong proponents suggests that alcoholism is either a complex medical social disease syndrome requiring a multipronged
 treatment approach or a very simple illness for which we have not yet discovered the remedy The latter may indeed be true
 but we cannot use what we do not know and must use what we do know We do however have the obligation to be responsible
 in our treatment to provide the best that is known at this time and to be discriminating in our prescription of appropriate
 treatment for individual patients If there is one conclusion we would like to offer in our preface it is that alcoholics
 constitute a markedly heterogeneous population with widely disparate needs for whom at least at our present level of
 knowledge a broad spectrum of treatment modalities is necessary If this is true then probably most of this book has validity
 With this volume on the treatment and rehabilitation of the chronic alcoholic we bring to completion our five volume series

The Biology of Alcoholism As the title of the present volume indicates we have departed from our original intention to deal solely with biological aspects of the syndrome and have attempted rather to produce a more comprehensive work

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